AD_____

Award Number: W81XWH-09-2-0064

TITLE:Effectiveness of Acupuncture in the Treatment of Gulf War Illness

PRINCIPAL INVESTIGATOR: Lisa Conboy

CONTRACTING ORGANIZATION: New England School of Acupuncture, Inc.
Newton, MA 02458

REPORT DATE: July 2010

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT:

Approved for public release; distribution unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	**2. REPORT TYPE**	**3. DATES COVERED** *(From - To)*
01-07-2010	Annual	1 JUL 2009 - 30 JUN 2010

4. TITLE AND SUBTITLE
Effectiveness of Acupuncture in the Treatment of Gulf War Illness

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-09-2-0064

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
DR. Lisa Conboy

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) AND ADDRESS(ES)
New England School of Acupuncture, Inc.
Newton, MA 02458

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The goals of the first year/ phase of the DOD funded research, GW080059, have been accomplished. We successfully gained IRB and administrative regulatory approval created our databases, instruments, and tested our procedures on mock volunteers which consisted of SurveyMonkey, the acupuncturists; initiated our advertising and most recently, our participant recruitment. The initial year of funding was spent primarily in extensive human subject review boards by NESA's contracted IRB, the New England Research Institute (NEIRB); IRB review for our biomarker collection and analysis through the Human Subjects Program Office of the Beth Israel Deaconess Hospital (BIDMC IRB); and the United States Army Medical Research and Materiel Command (USAMRMC IRB). All final approvals were granted this past month (July 2010), therefore advertising and recruitment has just begun. Upon completion of this project we should have important clinical information that will illustrate our outcome to increase the quality of life for veterans.

15. SUBJECT TERMS
No subject terms provided

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
U	U	U	UU	15	**19b. TELEPHONE NUMBER** *(include area code)*

Table of Contents

DOD Gulf War Illness Award Research Technical Reporting: 1 year Progress Report

GW080059 - Effectiveness of Acupuncture in the Treatment of Gulf War Illness

PI - Lisa Conboy, MA, MS, ScD

INTRODUCTION: This project is a single-blind randomized controlled clinical trial with a wait list control evaluating the effectiveness of individualized acupuncture treatment on subjects' overall health and disease burden. This three-year project collects main outcomes after 2 months of biweekly acupuncture treatment. Longer-term effectiveness will be measured with a 6 month follow-up. Our objectives are to find: a successful treatment of GWI, by gathering data to better understand: 1) the efficacy of acupuncture in treating GWI, 2) the mechanisms of how GWI may be helped by acupuncture. Our specific aim is to evaluate in a sample of veterans with GWI, the effectiveness of an individualized acupuncture treatment protocol on the subjects' GWI symptoms.

The study design utilizes a randomized controlled trial design with a wait-list-control. Volunteers will be randomly assigned to treatment or wait list arm using computer assignment. Our primary outcome is quality of life. In an effort to better understand this disease and its treatment we are considering psychosocial variables (quality of life, depression, anxiety, mood), fatigue, sleep quality, and pain. All of the measurement instruments used in this trial have been used before and published on in peer reviewed scientific journals. All have shown good validity and reliability.

BODY: The initial year of funding was spent simultaneously on extensive IRB review by NESA's contracted IRB, the New England Research Institute (NEIRB); IRB review for our biomarker collection and analysis through the Human Subjects Program Office of the Beth Israel Deaconess Hospital (BIDMC IRB); and the United States Army Medical Research and Materiel Command (USAMRCM IRB). Final IRB approval was granted just this month (July, 2010) by all three human subject review boards; therefore screening has just begun. We also recruited experienced study staff and study practitioners that successfully completed our study training. Concurrently we focused on the start up activities which included the formation of our final measurement procedure and instruments, the design of our databases and the testing of these procedures. A relational database was built for the purpose of intakes, screenings, and tracking. Our instrumentation package was created and placed onto *SurveyMonkey*, the WEB-based data collection interface. This interface was successfully created and tested on mock volunteers.

Since a single measure of severity that addresses all possible presentations of GWI does not exist we chose to use as the main outcome a general measure of health. Our primary outcome, the SF-36 is a 36-item measure of global health. It is well recognized with good reliability and validity; Items address multiple aspects of

physical and mental health as well as functionality. Almost 400 randomized controlled clinical trials suggest that the SF-36 is also a useful tool for evaluating the benefits of alternative treatments.

Several outlets have been utilized for recruitment of veteran volunteers for this study. Due to privacy regulations, the Veterans Administration (VA) was unable to provide the research team with the names of patients registered with the GWI registry. The Boston and Bedford VA systems were able however, to provide research staff with frequencies of GWI cases by zip code. By obtaining the frequency of GWI cases by zip code, the research team was able to identify cities and towns with large numbers of GWI cases, and therefore, the research team was able to select study acupuncturists practicing in close proximity to these potential subjects.

Additionally, outreach was performed to local veteran organizations and professional associations that are specific to veterans. Outreach efforts announcing the study to professional organizations included outreach to Dr. Roberta White and her staff at the Department of Environmental Health at Boston University. Her advice proved valuable to our recruitment efforts. Other professionals in the GWI field contacted included Dr. Robert Haley of Southwestern University, Dr. Gordon Broderick of the University of Alberta, Dr. Douglas Dockery of Harvard University, Dr. Harold Sox of Dartmouth University. We also contacted local veteran organizations including the U.S. Veterans Outreach Center; American Legion Department of MA; Veteran's of Foreign Wars of the U.S.; South Boston VFW Post 6536; Disabled American Veterans; Veteran's Up and Running, and Gulf War Vets of New England. IRB approved advertisement flyers were sent to these organizations as well as information sheets about the study. An IRB approved advertisement was placed in the local paper *Boston Metro* on 7/13/10. Additionally, a press release announcing the grant was distributed on 6/23/10 by NESA's public relations agency, Bishoff Communications, whom NESA has on monthly retainer. Several veterans contacted the research team expressing their interest as a result of press garnered from the release.

KEY RESEARCH ACCOMPLISHMENTS:

- Poster presentation at Southwest Symposium, April 2010 in Austin, TX on *Methodological Challenges in Designing Research Protocols to Evaluate Acupuncture in the Treatment of Complex Medical Diseases: the Case of Gulf War Illness* (please see attached slides).
- Poster presentation at The Society of Acupuncture Research, March 2010, Chapel Hill, NC. *Methodological Challenges in Designing Research Protocols to Evaluate Acupuncture in the Treatment of Complex Medical Diseases: the Case of Gulf War Illness* (please see attached poster).

REPORTABLE OUTCOMES:

- We have yet to publish any results as recruitment has just begun. Our hope is that once the study is underway it may represent a reportable outcome in year 2 of the funded work.

CONCLUSION:

We have just begun recruitment and our first medical screening day is scheduled for August 21st. We have our data collection and reporting systems in place and a well-trained experienced staff in operation. We hope to have reportable outcomes in the coming year.

REFERENCES:

1. Surveymonkey. http://www.surveymonkey.com. October 3, 2008.
2. McHorney CA, Ware JE Jr, Lu JF, Sherbourne CD. The MOS 36-item Short-FormHealth Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. *Med Care*. 1994;32(1):40-66.
3. Turner-Bowker DM, Bayliss MS, Ware JE Jr, Kosinski M. *Usefulness of the SF-8 Health* Survey for comparing the impact of migraine and other conditions. Qual Life Res. 2003;12(8):1003-12.

APPENDICES: See attached

Effectiveness of Acupuncture in Treating Gulf War Illness

Practitioner Training

Sunday, January 31, 2010
New England School of Acupuncture
Newton, MA

Presenters:

Lisa Conboy, MA MS ScD
Co-director of Research
Principal Investigator
lconboy@nesa.edu

Meredith St John, MAc LicAc
Academic Dean
Co-Investigator
mstjohn@nesa.edu

Gulf War Illness (GWI)

- Definition
- Epidemiology
- Study Methodology
- History
- Exposures to neurotoxicants
- GWI characterized by Traditional Chinese Medicine (TCM)
- First person accounts
- Clinical Partners
- Citations

Definition

- A chronic, multi-symptom illness (CMI)
- Affects more than one fourth of the nearly 700,000 U.S. military personnel who served in the first Gulf War Operation Desert Shield/Storm (1990-1991)
- CMI symptoms also studied in veterans in the United Kingdom, Canada, & Australia
- No disease-specific treatment identified as helpful

Symptoms in 3 clusters

Cluster A *Fatigability*	Cluster B *Mood & Cognition*	Cluster C *Musculoskeletal*
persistent fatigue 24 hrs or more after exertion	feeling depressed	joint pain/ muscle pain
	feeling irritable	
	feeling worried, tense or anxious	
	difficulty thinking	
	difficulty concentrating	
	problems finding words	
	problems sleeping	

Study Methodology

- Objectives: To find a successful treatment for GWI, by gathering data to better understand: 1) the effectiveness of acupuncture in treating GWI; 2) the mechanisms of this disease.
- Specific Aim: In a sample of veterans with GWI, evaluate the effectiveness of an individualized acupuncture treatment protocol on the volunteers' most distressing GWI symptom.

Study Methodology

- Unblinded randomized controlled trial design with a wait-list-control.
- Individualized treatments
- Active group→6 months of biweekly treatment
- Waitlist group→2 months of waiting then 4 months of weekly treatments

Study Methodology: How we measure improvement

Measure general symptoms in Quality of Life and most distressing symptoms

- Fatigability
  - fatigue 24 hours or more after exertion
- Mood and Cognition
  - feeling depressed or
  - feeling irritable or
  - difficulty thinking or concentrating or
  - feeling worried, tense, anxious or
  - problems finding words or
  - problems getting to sleep
- Musculoskeletal
  - joint pain or muscle pain

Study Methodology: How we measure improvement

- The SF-36
- Multidimensional Assessment of Fatigue
- The Profile of Mood States
- Pittsburg Sleep Quality Index
- Measure Your Medical Outcomes Profile
- Beck Anxiety Inventory
- McGill Pain Scale
- Carroll Depression Scale
- Social support, Social Networks, and Stress
- Medication use and Expectations for Treatment
- Blood draw to examine levels of selected markers of inflammation, stress, and immune function

Study Methodology How do we record TCM improvement

Recording TCM symptoms, diagnosis, prognosis, expectations for treatment, alliance with subject

- OM intake-baseline
- Health History Questionnaire-baseline
- Monthly progress TCM (baseline and monthly for 6 months of study)

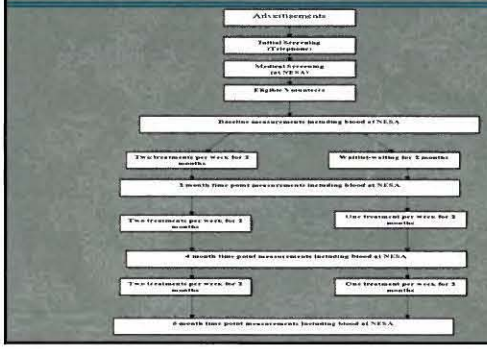
Study Methodology Patient Safety

- An **adverse event** is any health change (or side-effect) that happens to a volunteer while he/she is participating in the study.
- The PI has the primary responsibility of reporting adverse events to our Army safety team.
- Please contact study staff of any negative health change no matter how small.
- Please utilize 911 or suicide prevention hotline per your usual clinical protocol.

Study Methodology Practitioner Safety

- Safety issues treating trauma survivors
- Safety Resources
  - **Suicide Prevention Hotline**
    1-800-273-8255 (TALK)
  - **VA Boston**
    24-hour nurse available to provide telephone care for veterans
    1-800-865-3384
  - **National Veterans Helpline**
    1-800-507-4571

Recruitment/Randomization



Bombing of Baghdad

Persian Gulf

History

In the first Gulf War (Operation Desert Shield/Storm, 1990-1991), more troops were harmed by our own technology than by the enemy.

US Casualties	
Killed in action	148
Non-battle deaths	145
Wounded	458

Gulf War Illness
100,000 – 175,000

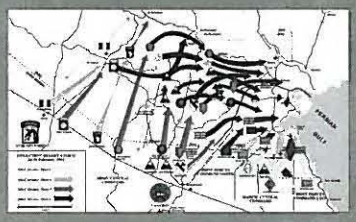
History

Timeline:

- **08/02/1990**
  - Saddam Hussein occupied Kuwait in 6 hours after a border dispute involving oil
- **Within days…**
  - US and coalition forces began massing troops & supplies in Saudi Arabia (Desert Shield) – 5 months
- **01/17/1991**
  - US began 43-day air war (Desert Storm)
  - Targeted electronic resources, radar, missiles, munitions… dropped more bombs than all of WWII
- **02/24/1991**
  - US began 100-hour ground war
  - Largest tank battle in history

Operation Desert Storm

Summary of the Offensive in the 4-Day Ground War



Operation Desert Storm

"Iraq went from the fourth-largest army in the world to the second-largest army in Iraq in 100 hours"

Lieutenant General Tom Kelly

Gulf War Illness

Many deadly harms of modern, technological warfare:

- Medication
- Pesticides

Exposures

"My unit arrived in the Gulf the day before the air war started. We first spent about a month in Dhahran in Saudi Arabia. Our chemical alarms went off several times during that month, and we had to go to MOPP-level four, which meant we had to put on chemical suits, masks, gloves, and boots.

"While we were still in Dhahran, we started taking pyridostigmine bromide (PB) pills, which were supposed to protect us against exposures to nerve gas. About three days after I started taking the pills, my eyes were blurry, my vision was jumping, and I was seeing double, and I was nauseated. By the fourth day, I was vomiting a little blood, so I went to sick-call. They told me to cut the dose in half and said there was nothing to worry about. At least I no longer vomited blood after I reduced the dosage. Many other people in the unit reported having similar vision problems."

SSgt P.B., Gulf War Veteran
(NAC 2004, p. 139)

US troops in protective gear

www.pbs.org/wgbh/pages/frontline/shadow/primer/groundwar.html (accessed 4/19/2010)

PB Exposure

Pyridostigmine Bromide (PB)

Numerous first person accounts provide details of side effects of PB that subsided after the medication was discontinued or the dosage reduced.

- Fever
- Diarrhea, gas, abdominal cramps, vomiting
- Weakness, muscle twitches, and spasms
- Fatigue
- Confusion, poor concentration
- Runny nose
- Blurred vision

PB Continued

Risk vs Harm

- Safe use for myasthenia gravis
- Investigational drug for pre-treatment for exposure to soman nerve agent
- High risk associated with possible chemical warfare

Dosage/exposure

- Dose-dependent relationship between use of PB and most severe symptoms, in ground troops serving in forward areas, living in open dessert

Pesticide Exposures

"On a nightly basis, we would spray our uniforms with pesticides. There was a chemical spray that they gave us to spray our uniforms. We had to hang them outside so that the excess spray would dissipate in the air, I guess. We weren't supposed to put them on immediately after spraying them.

"The sand fleas were a problem. We used to put flea collars around the legs of our cots or we would put flea powder on the floor around our cots to try to keep the sand fleas away from us while we were sleeping. We slept with nets over us to keep the flies off. The flies were ungodly."

SSgt T.S., Gulf War Veteran
(NAC 2004, p. 131)

Pesticide Exposures

Organophosphates

- **DEET, Dichlorvous pest strip**
- **Chlorpyrifos, Diazinon, Malathion used in surface spraying, environmental fogging**

Pesticide Exposures

Organophosphates a likely cause of GWI

- Result in delayed neuropathies (OPIDN) after acute poisoning episodes
- Suspected CNS effects from repeated low dose exposure even without acute episode
- Low level use linked to chronic neurogenerative disease and chronic multisymptom illness
- Role of biological variability of protective enzymes (paraxonase, or PON1) under investigation

Sarin Exposures

Sarin is classified as a nerve agent

- 100,000 troops exposed at Khamisiyah, Iraq
- Onset of symptoms after observing explosions of Iraqi missiles (Multiple Chemical Sensitivity)

Other Exposures

- Depleted uranium (DU) used in munitions and tank armor
- Oil fires and smoke
- Vaccines
- Sand and particulates
- Petrochemicals (tent heaters, jet fuel, solvents)
- Chemical agent resistant coating (CARC) paint
- Contaminated food and water
- Psychological stress

How TCM Characterizes GWI

TCM's individualized diagnosis and treatment strategy appropriate for heterogeneous presentation

- TCM Neurology
  - Wei-zhang (Flaccidity Syndrome) – treatment of organophosphate poisoning from TCM perspective
- Autonomic Nervous System (ANS)
- Bi Syndrome

TCM Treatments

Veterans with GWI will receive individualized TCM diagnosis and treatment strategy, directed at their most distressing symptom, and at any additional symptoms, as well as at their root condition; 1-2 x/week x 4-6 months. Full intake will include medical history and exposure to known or suspected neurotoxicants during the war

Treatments provided by senior practitioners in private offices, may include:

- needling with de qi sensation
- warming treatments, e.g., moxibustion, heat lamps
- manual therapies, including tui na, cupping,gua sha
- electroacupuncture, known to be helpful for its analgesic and anti-inflammatory effects
- microsystems - auricular and scalp
- press balls

TCM Treatments

Not within the scope of this study, excluded treatments are:

- Chinese Herbal Medicine (CHM)
- Supplements

Biomedical Treatments

Chronic Fatigue Syndrome (CFS)	exercise, cognitive-behavioral therapy (CBT)
Depression	antidepressants, psychotherapy, exercise
Fibromyalgia (FM)	no therapy identified as beneficial
Headache	medicate acute episodes, prophylactic care, behavioral
Irritable bowel syndrome (IBS)	antispasmodic medications, anti-depressants, cognitive-behavioral therapy (CBT)
Panic disorder	selective serotonin reuptake inhibitors (SSRIs) tricyclic antidepressants (TCAs), benzodiazepines (BZPs), CBT
Posttraumatic stress disorder (PTSD)	SSRIs, CBT

Biomedical Treatments

Medically unexplained physical symptoms (MUPS)

- Conservative diagnostic testing
- Judicious use of medications
- Collaborative goals
- Physical and role reactivation to reduce disability
- Social supports
- Coordination of care
- Psychiatric care only when specifically indicated
- Intensive multimodal care.

Clinical Partners

We invite practitioners of acupuncture and OM to collaborate with us and contribute to our knowledge base about GWI by sharing treatment results. If you have treated veterans with GWI, please consider writing case reports to share with us.

Please submit your case reports to:

dodgwi@gmail.com

Clinical Partners

Suggested format of case report:

- Abstract
- Description of the case – presenting symptoms, history, prior treatments & their effects, diagnosis, treatment strategy, treatment points, adjunctive techniques, effects of treatment
- Literature
- Discussion
- Summary or conclusions

Gulf War Illness

Special thanks & acknowledgements:

New England School of Acupuncture
150 California Street
Newton, MA 02458
www.nesa.edu

US Department of Defense
MEDCOM CDMRP W81XWH-09-2-0064

GWI Study Staff

- Lisa Conboy, MA, MS, ScD.: Principle Investigator
- Julie Dunn, Ph.D.: Data Analyst Coordinator/Recruitment Consultant
- Meredith St. John, MAc., LicAc.: Acupuncture Coordinator
- Rosa Schyer, LicAc., Senior Acupuncture Coordinator
- Marc Goldstein, MD: Medical Screener
- Jessica Wolin, MD: Medical Monitor
- Elaine Scarmoutzos: Project Coordinator
- Christina Noonan, LicAc.: Research Assistant
- Matthew Hilton, MD: Research Assistant
- Efi Kokkotou, MD: Biomarker Coordinator
- Roger Davis, Statistical Consultant
- Weihui Li: Work Study Student
- Kara Marquis: Work Study Student

Thank you
veterans!

Methodological Challenges in Designing Research Protocols to Evaluate Acupuncture in the Treatment of Complex Medical Diseases: the Case of Gulf War Illness

Lisa Conboy, MA MS ScD[1,2], Meredith St. John, MAc. LicAc. [1], Rosa Schnyer, LicAc[1], Julie Dunn, PhD[1]. [1]*New England School of Acupuncture,*
[2]Osher Research Center, Harvard Medical School

F6

Background

•The first Gulf War (Operation Desert Shield/Storm, 1990-1991), was initially considered a dramatic success with very few combat casualties. More troops were harmed by our own technology than by the enemy (RAC 2008, p. 214-228)*

•Today Gulf War Illness (GWI) is a chronic, multi-symptom illness (CMI), which affects more than one fourth of the nearly 700,000 U.S. military personnel who served. *

Three symptom clusters:

•Fatigability – Fatigue 24 hours or more after exertion
•Mood and Cognition – Feeling depressed or feeling irritable, sleep problems, difficulty thinking or concentrating, feeling worried, tense anxious, problems finding words
•Musculoskeletal – joint or muscle pain

How TCM Characterizes GWI

•TCM's individualized diagnosis and treatment strategy is appropriate for populations' heterogeneous presentation
GWI neurological presentations
•A new disease for TCM
•Wei-zhang (Flaccidity Syndrome) treatment of organophosphate poisoning
•Bi Syndrome
•Autonomic Nervous System (ANS) dysregulation

Study Methodology

Objectives: To find a successful treatment for GWI, by gathering data to better understand: 1) the effectiveness of acupuncture in treating GWI; 2) the mechanisms of this disease.

Specific Aim: Evaluate the effectiveness of an individualized acupuncture treatment protocol on the volunteers' most distressing GWI symptom.

Design:

•Unblinded randomized controlled trial with wait-list control
•Individualized treatments
•Active group – 6 months of biweekly treatment
•Waitlist group – 2 months of waiting then 4 months of weekly treatment

Multilevel Outcome Measures

•The SF-36
•Multidimensional Assessment of Fatigue
•The Profile of Mood States
•Pittsburg Sleep Quality Index
•Measure Your Medical Outcomes Profile
•Beck Anxiety Inventory
•McGill Pain Scale
•Carroll Depression Scale
•Social Support, Social Networks, and Stress
•Medication use and Expectations for Treatment
•Biomarkers

•Challenges:

•Unknown etiology
•Heterogeneous symptom
•presentation
•Individualized acupuncture treatments
•Appropriate control group

Clinical Partners

Practitioners: Do you treat veterans with GWI? Become our clinical partner by writing a short case report. Please contact Lisa Conboy lconboy@nesa.edu or Meredith St. John mstjohn@nesa.edu.

Thank you Veterans!!!

Funded by:
US Department of Defense
MEDCOM CDMRP W81XWH-09-2-0064

NEW ENGLAND SCHOOL OF ACUPUNCTURE

Study Staff

Marc Goldstein, MD: Medical Screener; **Jessica Wolin, MD**:Medical Monitor; **Elaine Scarmoutzos**, Project Coordinator; **Christina Noonan, MAc., LicAc.:** Research Assistant; **Matthew Hitron, MD**:Research Assistant; **Efi Kokkotou, MD:** Biomarker Coordinator; **Roger Davis PhD:** Statistical Consultant; **Wehui Li PhD:** Work Study Student; **Kara Marquis:** Work Study Student

* Research Advisory Committee on Gulf War Veterans' Illnesses. *Gulf War Illness and the Health of Gulf War Veterans: Scientific Findings and Recommendations*. Washington, D.C. US Gov't Printing Office, November 2008.